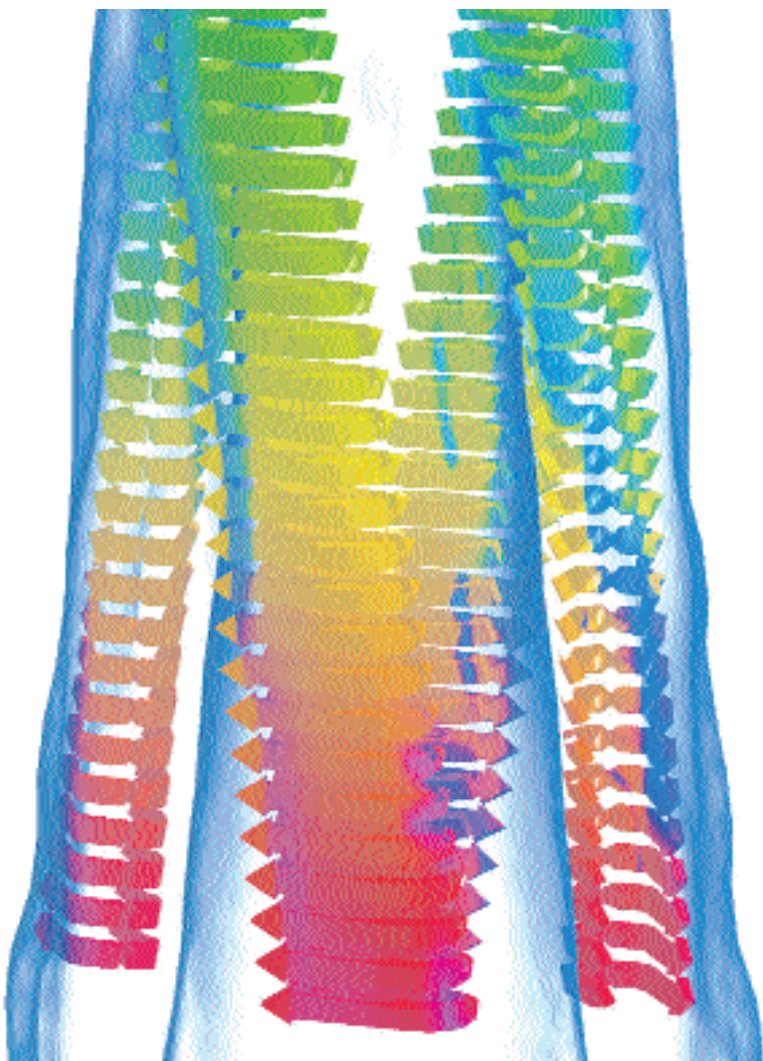




# The Institute of Structural Molecular Biology (ISMB)

at UCL/Birkbeck



# An introduction to the ISMB

## About the ISMB

The Institute of Structural Molecular Biology (ISMB) was created in July 2003 to:

- promote structural biology, proteomics, and chemical biology at UCL and Birkbeck
- foster closer links between the Department of Biochemistry & Molecular Biology at UCL, the School of Crystallography at Birkbeck, the Department of Chemistry at UCL, the School of Biological and Chemical Sciences at Birkbeck and the School of Computer Science and Information Systems at Birkbeck
- create an interface between UCL/Birkbeck structural and chemical biology and UCL biomedical research.

## Aims

The Institute of Structural Molecular Biology seeks to provide a scientific environment conducive to world-class research in the field of protein science. Our understanding of protein function increasingly depends on a deeper knowledge of the chemical and physical principles that govern protein behaviour (substrate recognition, catalysis, macromolecular interaction, etc). Work at the institute seeks to integrate the chemical and physical sciences to provide the molecular basis of protein function. The ISMB also seeks to exploit the knowledge of protein function to further our understanding of human diseases.

## ISMB Programmes

Members of the institute include some of the most productive UK scientists in the field of structural biology, chemical biology, biophysics, proteomics, and bioinformatics. Individual members have developed an impressive funding base totalling more than £46M in 2003.

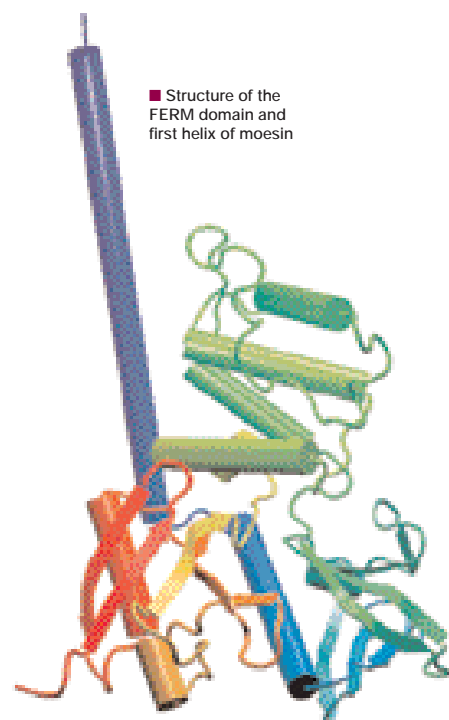
ISMB members participate in five main research programmes:

- Structural biology
- Chemical biology
- Biophysics
- Proteomics
- Bioinformatics.

## ISMB centres

Through its programmes, the institute also seeks to support and promote the creation of research centres. Each centre will interface with the larger biomedical community and provide services for biomedical researchers in the Bloomsbury area, in London, and the country as a whole. The centres which have been created so far are:

- The Bloomsbury Centre for Structural Biology
- The Bloomsbury Centre for Bioinformatics
- The Biophysics Centre
- The Chemical Biology Centre.



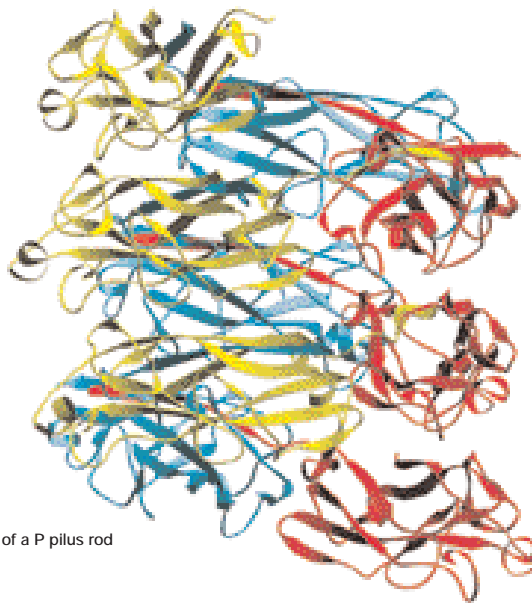
# An overview of the ISMB programmes and research centres

## Structural Biology programme

*Programme leader: Professor Helen Saibil*

The Structural Biology programme assembles a group of Principal Investigators (PIs) interested in using structural biology approaches as tools to elucidate the molecular basis of protein function and activity. Our broad spectrum of structural investigation techniques includes high-resolution electron microscopy, x-ray crystallography, and NMR. PIs in the Structural Biology programme not only benefit from state-of-the-art equipment that covers the entire spectrum of structure determination methods, but also from the unique interdisciplinary environment that the ISMB offers by linking its research programmes.

**Research Centre** The Structural Biology programme also runs the Bloomsbury Centre for Structural Biology (BCSB). For further details see [www.bcsb.lon.ac.uk](http://www.bcsb.lon.ac.uk).



■ Model of a P pilus rod

## Chemical Biology programme

*Programme leader: Professor Steve Caddick*

Laboratories participating in the Chemical Biology programme focus on the application of chemistry to the investigation of biological macromolecules and macromolecular interactions. Structural biology contributes essential information about the chemistry of the interfaces of interacting proteins. This information can in turn be exploited for the design of reagents interfering with or disrupting macromolecular interactions. On this basis, we design synthetic proteins and reagents, which can be used to provide a better understanding of biological processes.

**Research Centre** The Chemical Biology Centre (CBC) is in the process of being created under the leadership of Professor Steve Caddick. We anticipate the Chemical Biology Centre to be fully operational in 2006.

## Biophysics programme

*Programme leader: Professor John Ladbury*

The Biophysics programme studies the behaviour of biological macromolecules in solution and aims to elucidate the mechanisms and energetics of interactions between them. To carry out such investigations, we use a broad spectrum of techniques including microcalorimetry, fluorescence spectroscopy, analytical ultracentrifugation, circular dichroism, and surface plasmon resonance. Investigations of macromolecular interactions reveal the various molecular states that macromolecules must cycle through to perform their function and this complements structural biology work carried out at the ISMB.

**Research Centre** From September 2004 the Biophysics programme will run a Biophysics Centre, providing services to the wider research community.



## Bioinformatics programme

*Programme leader: Professor David Jones*

The overarching goal of bioinformatics research is the computational modelling of biological systems at various levels of complexity and detail. To achieve this, novel algorithms and methods along with fully integrated data resources need to be developed to solve important biological and medical problems. These developments will require close interaction between biological scientists, bioinformaticians, computer scientists, mathematicians, statisticians, physicists and researchers in other related disciplines.

The main bioinformatics themes relevant to the ISMB relate to the analysis and prediction of protein structure, along with methods for predicting protein-protein and protein-ligand interactions. Large scale application of these techniques to whole genomes and biological networks is facilitated by the use of large-scale distributed computing facilities, along with the associated grid software development.

**Research Centre** The Bioinformatics programme of the ISMB also runs the Bloomsbury Centre for Bioinformatics (BCB), which is expected to be fully operational by October 2004. The BCB will provide support and training resources in bioinformatics, and will also run a research incubator programme providing support for pilot projects expected to lead to full grant applications.

## Proteomics programme

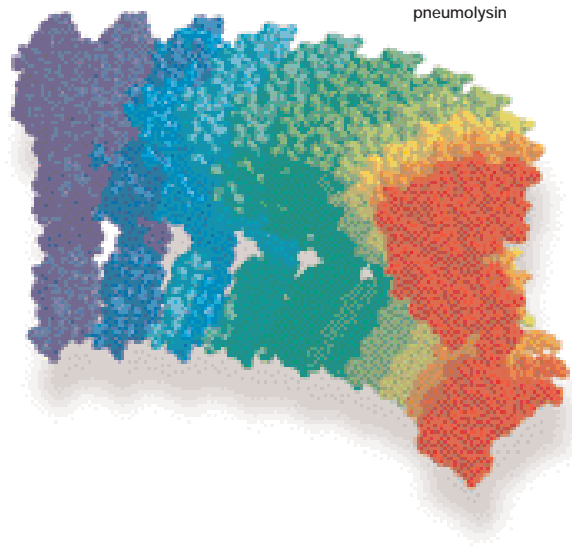
*Programme leader: Professor Jasminka*

*Godovac-Zimmermann*

The Proteomics programme uses changes in cellular proteomes to study parallel dynamic changes in cellular function, primarily in the area of cell signal transduction. New paradigms in cellular function suggest that many aspects of cellular function are controlled by rapid, stochastic, combinatorial processes which are linked to changes in cellular proteomes. We monitor and analyse the spatial and temporal properties of the molecular networks and fluxes involved in living cells by following the linked proteome changes.

New technologies developed in our laboratories and elsewhere, including gel and non-gel protein separations, parallel imaging processes, high throughput automatic protein identification, soft ionisation mass spectrometry and bioinformatics enable us to follow imprinting of the cellular proteome by functional processes. We are working on new technologies to increase sensitivity and proteome coverage. These include ultra-high sensitivity multi-photon-detection methods that allow linear quantitation of proteins upwards from zeptomoles and over ca.  $1E+8$  ranges of concentration. We identify proteins and characterize their phenotypic changes using high sensitivity MALDI, ion-trap and FTICR mass spectrometry.

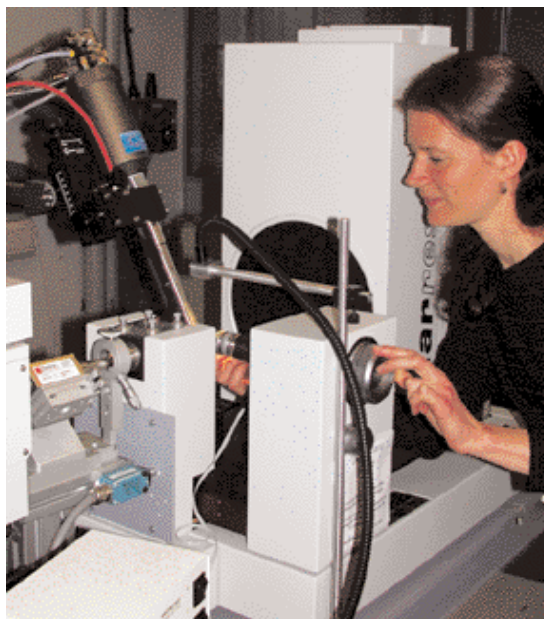
■ Model of a segment of membrane-surface bound ring of the bacterial toxin pneumolysin



# Facilities

## Facilities at the Institute of Structural Molecular Biology at UCL/Birkbeck

Researchers at the Institute of Structural Molecular Biology at UCL/Birkbeck enjoy access to state-of-the-art instrumentation in all fields covered by the institute. Large investments from the SRIF2 round of funding have afforded the creation of a Biophysics Centre which offers an array of investigating tools ranging from transient kinetics measurement apparatus (stopped- and quench-flow), steady-state measurements of protein activity and binding, to monitoring of macromolecular assemblies (analytical ultracentrifuge), conformational changes (circular dichroism, FTIR) and interaction thermodynamics (microcalorimetry).



■ X-ray detector at the ISMB X-ray crystallography facility

■ EM microscope at the ISMB electron microscopy facility



The institute is superbly equipped for cryo-EM and image reconstruction, with three cryo microscopes, including a 200 kV field emission gun system, and all the associated equipment for high resolution data collection and processing. A wide range of image processing systems is in routine use, including Spider and Imagic systems for single particle analysis. The NMR facility includes two high field 500 and 600 MHz NMR spectrometers, one of which is equipped with a cryogenically cooled probe system. Access to the NIMR National Facility 800/900 MHz spectrometers is routine. The Proteomics facility includes MALDI-TOF, ion-trap ESI, and FTICR mass spectrometers, and MALDI-TOF-TOF and (AP-)MALDI/ESI QTOF mass spectrometers. It is equipped with high throughput robotics for proteomics analyses. Finally, a JREI grant has funded a 132 processor high performance computing cluster for bioinformatics, image processing, and other computational activities.



# ISMB Membership

ISMB membership includes all research-active staff in affiliated departments. However, members active in Structural and Chemical Biology research as well as in Biophysics, Bioinformatics and Proteomics constitute the core-membership of the institute and are listed below.

## Bioinformatics

Professor Peter Coveney\*  
*UCL/Dept of Chemistry*

Professor David Jones\*  
*UCL/Dept Computer Science*

Dr Andrew Martin  
*UCL/Dept of Biochemistry & Molecular Biology*

Dr Nigel Martin  
*Birkbeck/School of Computer Science and Information Systems*

Professor Boris Mirkin  
*Birkbeck/School of Computer Science and Information Systems*

Dr Sylvia Nagl  
*UCL/Dept of Biochemistry & Molecular Biology*

Professor Christine Orengo\*  
*UCL/Dept of Biochemistry & Molecular Biology*

Dr Adrian Shepherd  
*Birkbeck/School of Crystallography*

Dr Lorenz Wernisch  
*Birkbeck/School of Crystallography*

## Chemical Biology

Professor Steve Caddick\*  
*UCL/Dept of Chemistry*

Dr Helen Hailes\*  
*UCL/Dept of Chemistry*

Professor Karl Hale  
*UCL/Dept of Chemistry*

Dr Stefan Howorka  
*UCL/Dept of Chemistry*

Dr Phillip Lowden  
*Birkbeck/School of Biological & Chemical Sciences*

Dr Charles Marson  
*UCL/Dept of Chemistry*

Dr David Selwood  
*UCL/WIBR*

Dr Alethia Tabor\*  
*UCL/Dept of Chemistry*

## Biophysics and Proteomics

Dr Rainer Cramer  
*UCL/Ludwig Institute*

Professor Jasminka Godovac-Zimmerman\*  
*UCL/Dept of Medicine*

Professor John Ladbury\*  
*UCL/Dept of Biochemistry & Molecular Biology*

Professor Steve Perkins  
*UCL/Dept of Biochemistry & Molecular Biology*

Professor Peter Rich  
*UCL/Dept of Biology*

Professor Bonnie Wallace\*  
*Birkbeck/School of Crystallography*

## Structural Biology

### X-ray crystallography

Dr Tracy Barrett  
*Birkbeck/School of Crystallography*

Dr Snezana Djordjevic\*  
*UCL/Dept of Biochemistry & Molecular Biology*

Dr Nicholas Keep\*  
*Birkbeck/School of Crystallography*

Dr Neil McDonald\*  
*Birkbeck/School of Crystallography*

Professor David Moss\*  
*Birkbeck/School of Crystallography*

Dr Renos Savva  
*Birkbeck/School of Crystallography*

Dr Christine Slingsby\*  
*Birkbeck/School of Crystallography*

Professor Gabriel Waksman\*\*  
*Birkbeck/University College London*

### NMR

Dr Andrew Dingley  
*UCL/Dept of Biochemistry & Molecular Biology*

Dr Paul Driscoll\*  
*UCL/Dept of Biochemistry & Molecular Biology*

### Electron Microscopy

Dr Carolyn Moores  
*Birkbeck/School of Crystallography*

Dr Elena Orlova  
*Birkbeck/School of Crystallography*

Professor Helen Saibil\*  
*Birkbeck/School of Crystallography*

## Other members of the ISMB Executive Committee include:

Professor Jeremy Brockes  
*UCL/Dept of Biochemistry & Molecular Biology*

Professor Richard Catlow  
*UCL/Dept of Chemistry*

Professor Elizabeth Hounsell  
*Birkbeck/School of Biological & Chemical Sciences*

Professor David Saggerson  
*UCL/Dept of Biochemistry & Molecular Biology*

Professor Elizabeth Shephard  
*UCL/Dept of Biochemistry & Molecular Biology*



# Contact details and essential information

## ISMB website

Further details about the ISMB, events and activities are available on the institute website.

[www.ismb.lon.ac.uk](http://www.ismb.lon.ac.uk)

## Contact

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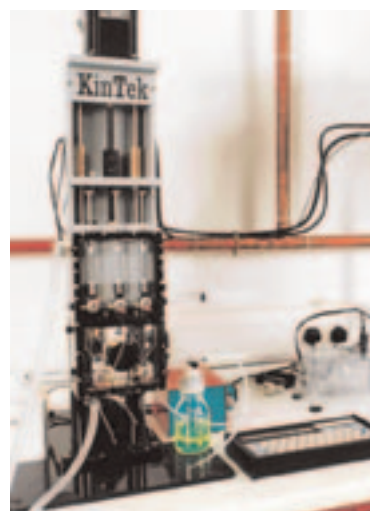
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■ Quench-flow equipment at the ISMB biophysics centre

